CASE REPORTS

Refer to: Mecikalski MB, Depner TA: Peritoneal dialysis for isopropanol poisoning. West J Med 1982 Oct; 137:322-325

Peritoneal Dialysis for Isopropanol Poisoning

MARK B. MECIKALSKI, MD
Salt Lake City

THOMAS A. DEPNER, MD
Sacramento, California

LITTLE ATTENTION has been given in recently published work to the toxicology and clinical features of isopropanol poisoning. Also, isopropanol intoxication has been successfully treated with hemodialysis,[1,2] but there has been little assessment of the effectiveness of peritoneal dialysis.[3] Because peritoneal dialysis is more readily available and easily administered, we report the peritoneal and total body clearance determinations of isopropanol during dialysis of a child who accidentally ingested this toxic alcohol. Following is a brief review of its toxic effects and metabolism.

Report of a Case

An 18-month-old male infant was admitted to hospital comatose. Earlier in the evening his babysitter saw him drink from a bottle of rubbing alcohol (70 percent isopropanol). The estimated volume ingested was 2.4 dl (8 oz). He vomited shortly afterward, appeared intoxicated and was taken to a community hospital emergency room where he was noted to be stuporous and having labored respirations. After vomiting again he was given naloxone hydrochloride, 0.2 mg intravenously; an endotracheal tube was placed and the infant was transferred to the University of California Davis Medical Center where he arrived three hours after drinking the rubbing alcohol.

His temperature was 36°C (96.8°F), pulse 124 per minute and blood pressure 90/40 mm of mercury. His weight was 9.5 kg (21 lb). He had no spontaneous respirations, did not respond to verbal or painful stimuli, and made no voluntary movements. Pupillary, corneal and gag reflexes were absent but deep tendon reflexes were normal.

Laboratory studies disclosed the following values: serum sodium 136, potassium 3.6, chloride 111 and bicarbonate 12 mEq per liter; blood urea nitrogen 23, glucose 276, acetone 51 and isopropanol 272 mg per dl. Arterial blood gas determinations done while the patient was receiving 100 percent oxygen via a respirator were as follows: oxygen partial pressure 396 mm of mercury, carbon dioxide partial pressure 28 mm of mercury and pH 7.29.

Treatment initially consisted of 20 mEq of sodium bicarbonate given intravenously and gastric lavage with a 0.9 percent saline solution until fluid returned clear, followed by administration of charcoal and magnesium sulfate. Because of the initially high isopropanol concentration and profound neurologic depression, peritoneal dialysis was started two hours after admission (five hours after ingestion). A standard commercial dialysate (Travenol) containing 132 mEq of sodium, 4.0 mEq of potassium, 106 mEq of chloride, 35 mEq of lactate, 3.5 mEq of calcium and 1.5 mEq of magnesium per liter and 1.5 mg of glucose per dl was cycled in 1,000 ml volumes every 30 minutes. A total of 13 cycles were run during 6½ hours. The subsequent clinical course correlated with blood and dialysate toxin levels is shown in Table 1. Isopropanol and acetone concentrations were measured with a Carle 211 analytical gas chromatograph by an established method.[4] Urine output was 170 ml from admission to the discontinuation of dialysis. Following dialysis the infant's weight was 9.4 kg and the serum creatinine level was 1.5 mg per dl, falling to a baseline of 0.5 mg per dl the following day.

Extubation was carried out 24 hours after admission, but it was necessary to reintubate due to upper airway edema. The second and final extubation was done a day later. Developmental assessment during this hospital stay showed a return to normal function. The total length of time in hospital was 12 days.

From the Division of Nephrology, Department of Internal Medicine, University of California Davis Medical Center, Sacramento. Dr. Mecikalski is now Pulmonary Fellow, University of Utah Medical Center, Salt Lake City, in the Division of Respiratory, Critical Care and Occupational (Pulmonary) Medicine.

Submitted, revised, August 20, 1981.

Reprint requests to: Thomas A. Depner, MD, Division of Nephrology, Department of Internal Medcine, UCD Medical Center, 4301 X Street, Sacramento, CA 95817.

TABLE 1.—*Summary of Clinical Recovery and Corresponding Levels of Isopropanol and Acetone in Blood and Dialysate*

Time After Ingestion (hr)		Isopropanol			Acetone		
		Blood (mg/dl)	Dialysate (mg/dl)	Peritoneal Clearance (ml/min)	Blood (mg/dl)	Dialysate (mg/dl)	Peritoneal Clearance (ml/min)
0	Ingestion	..	..	..	..	..	..
3	Admission, comatose, no pupillary reflex, respiration or movement	272	..	..	51	..	..
5	Dialysis started	..	..	..	..	..	..
5½		..	33	..	..	22	..
6½	Pupils sluggishly reactive	..	..	..	..	..	..
8		62	19	10.2	73	30	13.7
9½	Spontaneous respirations, able to be aroused	..	..	..	..	..	..
10½		27	7	8.6	80	31	12.9
11	Limb restraints necessary	..	..	..	..	..	..
11½	Dialysis discontinued	..	..	..	..	..	..
14½	Making purposeful movements	<5	..	..	91	..	..

Discussion

Although about 10 percent of isopropanol may be converted to the glucuronide,[5] the major pathway of metabolism is via alcohol dehydrogenase to acetone.[6] A case of a confused or comatose patient having acetonuria in the absence of glycosuria, especially without evidence of starvation, should suggest a toxic reaction to isopropanol. An unexplained rise in serum osmolality may call attention to the presence of a foreign substance, and might be used as an estimate of isopropanol concentration if an accurate assay is not available and if it is certain no other substance has been ingested. Acetonemia may reach significant quantities[1,3] and exacerbate a toxic condition, as its effects are similar to ethanol at equal blood concentrations.[7,8(p123)] Its rate of metabolism is much slower, however,[7,9] which probably accounts for the continued slow increase in blood acetone content in this patient even though blood isopropanol content was decreasing. This behavior of isopropanol and acetone concentrations has been seen in experiments with animals.[6,9]

Isopropanol quantities in body fluids are best measured by a gas chromatographic method. Users of alcohol dehydrogenase testing methods may be misled by ethanol[10] and earlier researchers using a modification of an iodometric assay for ethanol may have been misled by acetone.[11] In most cases of toxic ingestions in which coma occurred, blood concentrations were greater than 125 mg per dl,[1,2,12-15] with some patients who died having measurements at 150 mg per dl.[16] One infant survived, receiving supportive therapy alone, with a level of 520 mg per dl.[12] It must be noted that the methods used to assay for isopropanol were not specified in any of these reports, nor were acetone levels routinely measured.

The volume of distribution of isopropanol is 0.7 to 0.8 times body mass, similar to ethanol.[17,18] The rate of metabolism of isopropanol is proportional to its concentration and follows simple first-order kinetics.[9] This contrasts with ethanol which saturates its metabolic mechanisms at very low levels and therefore usually declines at a linear rate independent of concentration.[19]

The blood content of isopropanol given in Table 1 follows an exponential rate of decline, with an elimination constant during dialysis of 33 percent per hour. Assuming a volume of distribution of 7.1 liters the total body clearance of isopropanol during dialysis is 39 ml per minute, to which peritoneal dialysis contributes 9.4 ml per minute or approximately a fourth. The nondialysis or metabolic elimination constant is 25 percent per hour and compares favorably with previously reported values for dogs and rats of 17 percent and 35 percent per hour respectively.[9] Assuming these clearances and the volume of distribution of isopropanol to be constant, the blood concentration at the start of dialysis can be estimated to be 167 mg per dl and the maximum level before admission to be about 400 mg per dl. The latter quantity correlates with the profound degree of neurologic depression we observed.

Isopropanol is most widely encountered in a 10 percent solution sold as rubbing alcohol, but it may also be found in cosmetics, mouth washes, hair tonic, skin disinfectants, deicers, antifreeze and solvent mixtures.[20] Absorption from the gut is rapid and complete. Using isolated segments of gastrointestinal tract from dogs, Wax and coworkers[21] determined the absorption of a dose of 1.25 ml per kg of body weight (as a 10 percent solution) in stomach, duodenum and jejunum to be 41 percent, 67 percent and 91 percent, respectively, at 30 minutes. In jejunoileal loops absorption was 99 percent complete in two hours.

Symptoms and signs of a toxic reaction to isopropanol are generally similar to those seen with ethanol, though isopropanol probably does not produce an initial stage of stimulation.[20] Symptoms of a toxic reaction include dizziness, incoordination, headache, confusion, stupor, coma, hypothermia, aspiration and respiratory arrest. Gastroenteritis, more prominent than that usually seen with ethanol poisoning, may occur.[8(pp185-188)] Hypotension is a bad prognostic sign.[16] Renal failure has been reported possibly as a result of hypotension[16,22] or rhabdomyolysis.[23] Postmortem studies have shown hemorrhagic gastritis, hemorrhagic tracheobronchitis and pulmonary edema but no specific changes.

Studies with animals have shown that isopropanol is about 1½ to 2 times as toxic as ethanol. The certain lethal dose for a 70-kg (154-lb) human would then be about 500 ml of pure alcohol or 25 oz of 70 percent rubbing alcohol.[24,25] In one study it was noticed that deaths from isopropanol occurred considerably later than those from ethanol.[25] Both death[16] and survival[23] have been reported with presumed ingestion of 4.7 dl (16 oz) of rubbing alcohol. Two cases of isopropanol poisoning have been described in infants receiving alcohol baths for fever.[13,14] The route of absorption was presumably inhalation as large amounts of isopropanol applied topically to animals have had little effect.

After gastric lavage it is reasonable to attempt to hasten recovery from isopropanol intoxication, especially in comatose or hypotensive patients, but the medical urgency is not as great as that for methanol intoxication where permanent neurologic damage may occur due to the production of formaldehyde and formic acid. Similarly, ethylene glycol, whose metabolite oxalic acid is very corrosive and a potential cause of renal failure, should be removed promptly. Ethanol, isopropanol and their metabolites have lower intrinsic toxicities than methanol and ethylene glycol metabolites. Supportive therapy rather than an attempt to promote active excretion may be adequate for the former substances, whereas rapid removal of methanol and ethylene glycol is much more important. Isopropanol poisoning alone probably is not alleviated by activated charcoal administration if its adsorption characteristics roughly parallel those of ethanol, which is adsorbed in amounts of about 0.5 gram per gram of charcoal.[26,27] Because relatively large amounts of these alcohols are necessary to produce toxic effects, the quantity of charcoal administered would have to be correspondingly great. It would also need to be administered soon after the alcohol ingestion, as isopropanol is absorbed so rapidly in the gut.

Hemodialysis has been shown to be effective for removal of both ethanol and methanol in humans and clearances have approached 150 ml a minute in vitro.[19] Limited studies have shown that hemodialysis is also effective in lowering blood quantities of isopropanol, which in turn accelerates recovery of intoxicated patients.[1,2] Urine levels of isopropanol closely parallel those in the blood,[1] indicating that it is not substantially concentrated in the urine and that forced diuresis would be relatively ineffective. As an example, a daily urine flow equal to the total body water volume would require about 16 hours to merely halve the initial isopropanol concentration.

In this normotensive patient who had no evidence of hepatic disease, peritoneal dialysis, though effective in removing isopropanol, accelerated endogenous removal rates by only 30 percent and contributed little to the observed decline in isopropanol concentration in urine. However, peritoneal acetone clearance was substantial, approximately equivalent to expected pulmonary clearance, and may have hastened central nervous system recovery.

REFERENCES

1. Freireich AW, Cinque TJ, Xanthaky G, et al: Hemodialysis for isopropanol poisoning. N Engl J Med 1967 Sep 28; 277:699-700
2. King HL Jr, Kent PB, Shires DL: Hemodialysis for isopropyl alcohol poisoning. JAMA 1970 Mar 16; 211:1855
3. Dua SL: Peritoneal dialysis for isopropyl alcohol poisoning (Letter). JAMA 1974 Oct 7; 230:35
4. Sunshine I: Methodology for Analytical Toxicology. Boca Raton, FL, CRC Press, 1975, pp 149-154
5. Williams RT: Detoxication Mechanisms, 2nd Ed. New York, John Wiley & Sons, 1959, pp 63-65
6. Nordmann R, Ribiere C, Rouach H, et al: Metabolic pathways involved in the oxidation of isopropanol into acetone by the intact rat. Life Sci 1973 Oct; 13:919-931
7. Haggard HW, Greenberg LA, Turner JM: The physiological principles governing the action of acetone together with determination of toxicity. J Ind Hyg Toxicol 1944 May; 26:133-151
8. Gosselin RE, Hodge HC, Smith RD, et al: Clinical Toxicology of Commercial Products, 4th Ed. Baltimore, Williams & Wilkins, 1969
9. Abshagen U, Rietbrock N: Kinetik der Elimination von 2-Propanol und seines Metaboliten Aceton bei Hund und Ratte. Naunyn Schmiedebergs Arch Pharmacol 1969; 264:110-118
10. Vasiliades J, Pollock J, Robinson CA: Pitfalls of the alcohol dehydrogenase procedure for the emergency assay of alcohol: A case study of isopropanol overdose. Clin Chem 1978 Feb; 24:383-385

11. Widmark EMP: Eine Mikromethode zur Bestimmung von Athylalkohol im Blut. Biochem 1922; 131:474-483

12. Visudhiphan P, Kaufman H: Increased cerebrospinal fluid protein following isopropyl alcohol intoxication. NY State J Med 1971 Apr 15; 71:887-888

13. Garrison RF: Acute poisoning from use of isopropyl alcohol in tepid sponging. JAMA 1953 May 23; 152:317-318

14. Senz EH, Goldfarb MD; Coma in a child following use of isopropyl alcohol in sponging. J Pediatr 1958 Sep; 53:322-323

15. McCord WM, Switzer PK, Brill HH: Isopropyl alcohol intoxication. South Med J 1948 Jul; 41:639-642

16. Adelson L: Fatal intoxication with isopropyl alcohol. Am J Clin Pathol 1962 Aug; 39:144-151

17. Newman HW, Lehman AJ: Rate of disappearance of alcohol from the blood stream in various species. Arch Intern Pharmacodyn 1937; 55:440-446

18. Makar AB, Mannering GJ: Kinetics of ethanol metabolism in the intact rat and monkey. Biochem Pharmacol 1970 Jun; 19:2017-2022

19. Marc-Aurele J, Scheiner GE: The dialysance of ethanol and methanol: A proposed method for the treatment of massive intoxication by ethyl or methyl alcohol. J Clin Invest 1960; 39:802-807

20. Browning E: Toxicity of Industrial Organic Solvents, 2nd Ed. London, Her Majesty's Stationery Office, 1953, pp 335-341

21. Wax J, Ellis FW, Lehman AJ: Absorption and distribution of isopropyl alcohol. J Pharmacol Exp Ther 1949 Oct; 97:229-237

22. Chapin MA: Isopropyl alcohol poisoning with acute renal insufficiency. J Maine Med Assoc 1949; 40:288

23. Juncos L, Taguchi JT: Isopropyl alcohol intoxication. JAMA 1968 May 20; 204:732-734

24. Lehman AJ, Chase HF: The acute and chronic toxicity of isopropyl alcohol. J Lab Clin Med 1944 Jun; 29:561-567

25. Morris HJ, Lightbody HD: The toxicity of isopropanol. J Ind Hygiene Toxicol 1938 Jun; 20:428-434

26. Holt EL Jr, Holz PH: The black bottle—A consideration of the role of charcoal in the treatment of poisoning in children. J Pediatr 1963 Aug; 63:306-314

27. Smith RP, Gosselin RE, Henderson JA, et al: Comparison of the adsorptive properties of activated charcoal and Alaskan montmorillonite for some common poisons. Toxicol Appl Pharmacol 1967; 10:95-104

Refer to: Wagner GM, Liebhaber SA, Cutting HO, et al: Hematologic improvement following splenectomy for hemoglobin-H disease. West J Med 1982 Oct; 137:325-328

Hematologic Improvement Following Splenectomy for Hemoglobin-H Disease

GAIL M. WAGNER, MD
Oakland, California

STEPHEN A. LIEBHABER, MD
San Francisco

HUNTER O. CUTTING, MD
Oakland, California

STEPHEN H. EMBURY, MD
San Francisco

THE RECENT INFLUX of Southeast Asians into the United States has provided the American medical community with a host of unfamiliar medical problems, mainly hemoglobinopathies and infections. The patient in this report has a form of α-thalassemia, a hemoglobinopathy that is highly prevalent in Asia, having a frequency of 4 percent in China and 20 percent in Thailand.[1] The genetics and molecular mechanisms of α-thalassemia have been well reviewed.[1-7] Normally, the α-chain of the hemoglobin molecule has four α-globin structural genes ($\alpha\alpha/\alpha\alpha$)[8-10] that are located at two genetic loci.[11,12] Either gene deletion[8-12] or a dysfunctional nondeletion lesion[7,11,13] can result in a thalassemic α-globin gene. When only a single normal α-globin gene is present ($--/-\alpha$) the clinical result is hemoglobin-H (HbH) disease, which is characterized by moderately severe hemolytic anemia, microcytosis and splenomegaly. A mutant gene coding for the elongated α-globin chain of the electrophoretically slowly migrating hemoglobin Constant Spring (HbCS) mimics a thalassemic α-globin gene in that HbCS is present in very low amounts.[14-16] Thus, the clinical syndrome of HbH disease is seen also with the presence of one normal α-globin gene and an α^{CS}-globin gene.[14] HbCS is found in 40 percent of Southeast Asians with HbH disease.[17]

Herein we report the case of a young Cambodian woman who underwent splenectomy resulting in successful relief of the symptoms of anemia due to HbH disease associated with HbCS. The anemia of HbH disease is related to decreased synthesis of α-globin and of total hemoglobin[18,19] and to hemolysis, a result of unbalanced globin synthesis,[20] that occurs mainly in the spleen.[21] Thus, the intent of splenectomy in this patient was to diminish the peripheral hemolytic component of the anemia. When last reviewed in the 1960's, the efficacy of this procedure was uncertain.[21,22-24] Accordingly, we did a complete hematologic assessment both before and after the operation to evaluate the patient's response to splenectomy.

Report of a Case

A 24-year-old woman who recently immigrated to this country from Cambodia was admitted to Highland General Hospital in July 1980 for evaluation of dizziness, weakness, dyspnea and dis-

From the Department of Medicine, Highland General Hospital, Oakland, California; the Hematology Unit of the Medical Service, San Francisco General Hospital Medical Center, and the Howard Hughes Medical Research Institute and the Department of Medicine, University of California, San Francisco.

Submitted, revised, August 14, 1981.

Reprint requests to: Stephen H. Embury, MD, Building 100, Room 263, San Francisco General Hospital, San Francisco, CA 94110.